Systemic and Local Delivery of High-Molecular-Weight Drugs by Powder Inhalation

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The pulmonary route has recently attracted attention as a noninvasive administration route for high-molecular-weight drugs. In the present study, we prepared insulin powder and pCMV-Muβ powders for inhalation for systemic and local therapy, respectively. Citric acid was effective to increase pulmonary insulin absorption in rats from powders prepared by spray-drying technique with mannitol as a vehicle. However, citric acid deteriorated the stability of insulin. A combination of insulin powder and citric acid powder improved the stability without losing the enhancing activity. Insulin powders of various concentrations in mannitol were prepared by the SCF process. Interestingly, decrease in mannitol content resulted in increased efficacy of the powders and the most potent powder among the insulin powders examined was that prepared by the SCF process with no additives. Next we prepared plasmid DNA powders with mannitol by the SCF process. Chitosan was added as a non-viral vector. The expression of luciferase after the pulmonary administration of pCMV-Luc powder in mice was maximized when the N/P ratio was 5. Powders of pCMV-Muβ, a plasmid DNA encoding murine interferon β, with chitosan and mannitol was intratracheally administered to murine lung metasitatis models which were prepared by the intravenous injection of CT-26 mouse colon carcinoma cells. The pCMV-Muβpowders suppressed the increase in lung weight and number of nodules and prolonged the survival of the mice with smaller dose of pCMV-Muβ than pCMV-Muβ solutions. Intratracheal administration was more effective than intravenous administration. These findings suggested that the pCMV-Muβ powders had high therapeutic potential in murine lung metastasis model.